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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,794	08/21/2003	Andrew J. Bett	20699Y	8205

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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,794	BETT ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,21-23 and 84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 21-23 and 84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to the Request for Continued Examination filed 10/15/2007. The status of the claims is as follows: claims 1-11, 21-23 and 84 are under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 contains the trademark/trade name PER.C6 ®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a specific cell line and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 21 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat 6475480 (hereinafter as "Mehtali et al), US Pat 5849561 (hereinafter as "Falck-Pederson") and US Pat 7026164 (hereinafter as "Li et al"). *All references have been previously cited.* The limitations of the claims rejected above are as follows: 1. a method for propagating replication- defective adenovirus in a El-complementing cell line where the adenoviral E1 complementing cell line expresses an E1 gene product which is not of the same serotype as the replication-defective adenovirus; inserting all or a portion of heterologous E4 region which includes the ORF6 into a replication-defective adenovirus; the heterologous E4 region is of the same

serotype as the E1 serotype; and introducing the replication-defective adenovirus into the adenoviral E-1 complementing cell line, allowing propagation and rescuing the propagated adenovirus; 2. wherein the heterologous adenoviral E4 is the complete region; 3. wherein the heterologous E4 comprises the complete E4 region and native E4 promoter; 4. wherein the E4 region is inserted into the replication defective adenovirus in place of sequence encoding ORF6; 5. wherein the heterologous E4 region is inserted into the replication defective adenovirus in place of sequence encoding the complete adenoviral E4-encoding region; 6. wherein the heterologous a.denoviral E4 region is derived from a subgroup C adenovirus, more specifically, of serotype 5; 7. wherein the replication defective adenovirus is an adenovirus of subgroup B, more specifically, of serotype 35; 8. wherein the heterolgous adenoviral E4 region is operatively linked to a heterologous promoter; 9. wherein the adenoviral El-complementing cell line is a PER.C6 cell line; and 10. wherein the gene of interest is inserted into an E-1 deleted region.

Mehtali et al describe the use of a polynucleotide encoding one or more ORF(s) of the E4 region (see Abstract), including the use of heterologous E4 sequences (col.4, lines 35-41, col. 7, lines 55-56 and col. 9, lines 35-38) in replication defective adenoviruses "to improve the expression and/or persistence of expression of a recombinant gene in a host cell or organism" (see column 1). A complementation cell line is used to complement the E1 function (see column 10). The gene of interest may be inserted in place of the deleted E1 sequence in an E1- adenoviral vector (see column 9). Also, this prior art reference recites the following "the invention describes the

use of a polynucleotide encoding one or more ORF(s) of the E4 region of an adenovirus selected from ORF1, ORF2, ORF3, ORF4, ORF3/4, ORF6/7, ORF6 and ORF7 taken individually or in combination, to improve the expression and/or persistence of expression of a gene of interest operably linked to regulatory elements and inserted into an expression vector" (Abstract). Both homologous and heterologous E4 promoters are taught by Mehtali et al (see paragraph 37). Mehtali et al further disclose the following recitation: "In a particularly preferred embodiment the vector into which the polynucleotide comprising the E4ORFs are inserted, is an adenoviral vector, preferably one from which the E4 region has been deleted" (paragraph 41). The following recitation by Mehtali et al reveals the placement of the heterologous E4 region: "it is also possible that the vector is constructed by deleting all E4 sequences, in particular all E4ORFs, and inserting certain E4ORFs from the same or other adenovirus backbones in the adenoviral vector at a location where the E4 region normally resides or at a different location, e.g. in place of the deleted E1 or E3 region (paragraph 16). Lastly, Mehtali et al teach providing E4ORF *in cis* or *trans* to an E4 deleted vector carrying a transgene (paragraph 14). This reference reveals that impaired transgene expression in E4-deleted adenoviral vectors could be fully restored by the presence and expression of certain E4ORFs and that the E4 region may very between the different adenovirus strains (column 3). This reference does not explicitly express using different serotypes of the adenovirus. Further, Mehtali et al do not disclose using the PER.C6 cell line.

Falck-Pedersen discloses a method of producing a replication deficient adenovirus in which the virus is deficient in both E1 and E4 functions. The adenovirus is

produced in a cell that provides *in trans* the gene functions of the E1 and E4 regions of an adenovirus "not belonging to the same serogroup as the replication deficient adenovirus" (see Abstract). The replication deficient adenoviruses to be propagated as disclosed by Falck-Pedersen include those from groups A, B (includes Ad35), D, E and F while using a cell line that complements the essential gene function of the group C adenoviruses, including Ad 5 (see column 10 and Examples 1-8). Further, Falck-Pedersen discloses that the essential gene function of the E4 region are harmful to the host cell and a regulable promoter may be useful so that the gene function of the E4 region can be provided only when the replication deficient adenovirus is in need of the toxic gene products for its replication. This prior art reference also discloses the following recitation: "The ability to functionally interact appears to be absolutely conserved within a serotype, but less conserved between differing serotypes of a serogroup, and nonconserved between viruses of differing serogroups. Thus, it will be readily appreciated that in some embodiments of the present invention it is preferable for the essential gene products of the E1 and E4 regions of the adenoviral genome to be derived from the same serogroup, and even more preferable for them to be derived from the same serotype" (column 8). Falck-Pedersen reveals the following finding in Example 6: "this example demonstrates that the provision of a gene function of the E4 region of the adenoviral genome in addition to the essential gene functions of the E1 region of the adenoviral genome surprisingly increases the efficiency of complementation of E1 deficient adenoviruses when the E1 gene products provided in

trans are obtained from an adenovirus of a serogroup different from that of the replication deficient adenovirus" (columns 14-15).

The above references do not teach using the adenoviral El-complementing cell line PER.C6. Li et al disclose a packaging cell line, PER.C6, used for the production of recombinant adenoviral vectors and replication defective adenoviral vectors with E1 early gene region deletion (see Abstract).

Therefore, it would have been obvious for one of ordinary skill in the art to modify the teachings of Mehtali et al, Falck-Pedersen, and Li et al to make a method with the above claim limitations. One would have been motivated to combine the teachings of Falck-Pedersen and Mehtali et al because the teachings both reveal an enhanced production of replication deficient adenovirus by either using distinct serotypes as taught by Falck-Pedersen or preventing impaired transgene expression as taught by Mehtali et al. Further, one would have been motivated to use PER.C6 cells in order to reduce unwanted recombination events between the cell line and vector as suggested by Li et al (col. 2, 17-38). The ordinary artisan would be motivated to combine the teachings to obtain optimal results. There would have been a reasonable expectation of success, given that the cell line and the underlying molecular biology techniques were commonly used in the art for the production of adenovirus. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-11, 21-23 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat 5849561 (hereinafter as "Falck-Pederson"), US Pat

7026164 (hereinafter as "Li et al") and US Pat 6475480 (hereinafter as "Mehtali et al), and further in view of Megede et al (2000). *All references have been previously cited.* The limitations of the above claims are: 1. a method for propagating replication-defective adenovirus in a El- complementing cell line where the adenoviral E1 complementing cell line expresses an E1 gene product which is not of the same serotype as the replication-defective adenovirus; inserting all or a portion of heterologous E4 region which includes the ORF6 into a replication-defective adenovirus; the heterologous E4 region is of the same serotype as the E1 serotype; and introducing the replication-defective adenovirus into the adenoviral E-1 complementing cell line, allowing propagation and rescuing the propagated adenovirus; 2. wherein the gene of interest encodes an HIV-1 antigen, more specifically, HIV-1 gag antigen.

As discussed above, the limitations of claims 1-11, 21 and 84 has been met by the teachings of the following prior art references: Falck-Pederson, Li et al and Mehtali et al. These references, however, do not disclose propagating HIV-1 gag antigen as a gene of interest. Megede et al teach that gag is believed to be an important target for the host cell-mediated immune control of the virus during natural infection (see Abstract). It would have been obvious to one of ordinary skill in the art to use the HIV-1 gag as the gene of interest in the method. One would have been motivated to do so in order to express gag proteins for vaccines as disclosed by Megede et al (see Abstract). There would have been a reasonable expectation of success given the gene has been characterized and the underlying techniques are widely known and commonly used.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been considered to the extent that they apply to the new grounds of rejection. Briefly, Applicant submits that there is no motivation to combine the applied prior art teachings. This is not found persuasive; see rejection above which discusses the enhancement disclosed by Mehtali et al and Falck-Pedersen in a replication deficient adenovirus. Thus, one would combine the teachings to obtain optimal results.

Conclusion

NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michelle Horning
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